ORIGINAL ARTICLE

Outcome of Primary Percutaneous Coronary Intervention in Octogenarians with Acute Myocardial Infarction

*Yi-Chih Wang,[1] Juey-Jen Hwang,[1,2] Chi-Sheng Hung,[2] Hsien-Li Kao,[2] Fu-Tien Chiang,[2] Chuen-Den Tseng[2]**

Background/Purpose: Acute myocardial infarction (AMI) results in more complications and increased mortality in octogenarians compared to patients in younger age groups. This study investigated the short- and long-term outcomes in octogenarians after primary percutaneous coronary intervention (PCI).

Methods: During the study period from May 1997 to August 2004, 54 patients ≥ 80 years old with ST-elevation myocardial infarction (STEMI) were eligible for primary PCI. Data collected included baseline clinical characteristics and usage of cardiovascular medications. Diagnostic coronary angiography and revascularization procedures were performed using standard practices. During hospitalization, the clinical course including serial changes in cardiac enzymes, adverse events associated with myocardial infarction or treatment, and inhospital or long-term mortality of patients were recorded.

Results: The mean age of the 54 patients (35 men, 19 women) was 82.8 ± 2.5 years (range, 80–89 years). Among them, 27 (50%) had anterior infarction, six (11%) had anterolateral infarction, and 21 (39%) had inferior infarction, inclusive of three patients with accompanying right ventricular infarction. Among them, 20 (37%) patients were in Killip class I, nine (17%) were in class II, two (4%) in class III, and 23 (43%) in class IV. The mean delay from onset of symptoms to arrival in hospital was 220 ± 167 minutes, and 189 ± 169 minutes from hospital arrival to reperfusion. Diagnostic coronary angiography revealed that 48 (89%) patients had multivessel disease. Inhospital death occurred in 23 (43%) patients, with the leading causes of death being profound cardiogenic shock (61%), and free wall rupture (26%).

Conclusion: Octogenarian patients who developed STEMI tended to have multivessel disease. These patients had a high inhospital mortality rate that was most likely to be due to cardiogenic shock. [*J Formos Med Assoc* 2006;105(6):451–458]

Key Words: acute myocardial infarction, octogenarian, primary percutaneous coronary intervention

There is a high prevalence of coronary artery disease in octogenarians (≥ 80 years old),[1] and they are also the fastest growing segment of the population. In the United States, over 50% of acute myocardial infarctions (AMIs) occur in people older than 65 years, and 80% of those who die from AMI are more than 65 years old.[2] A population-based study conducted between 1975 and 1995 found that patients aged 75–84 and ≥ 85 years had 7.8 and 10.2 times greater risk of dying from AMI during hospitalization than patients younger than 55 years.[3] Age is a strong independent predictor of outcomes, including inhospital and post-hospital mortality rates, in patients with AMI[4,5] because of its association with increased severity of coronary atherosclerosis, reduced car-

[1]Cardiovascular Division, Department of Internal Medicine, National Taiwan University Hospital Yun-Lin Branch, Yun-Lin, and [2]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan.

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***Correspondence to:** Dr. Chuen-Den Tseng, Department of Internal Medicine, National Taiwan University Hospital, 7, Chung-Shan South Road, Taipei 100, Taiwan.
E-mail: cdtseng@ha.mc.ntu.edu.tw

diac reserve and multiple comorbidities.[6,7] Early reperfusion via primary percutaneous coronary intervention (PCI) or thrombolytic therapy is the cornerstone of effective treatment for patients with ST-elevation myocardial infarction (STEMI).[8] However, there are many limitations to thrombolytic therapy in the older population, and some studies have suggested that primary PCI is superior to thrombolytic therapy and leads to a lower rate of hemorrhagic stroke[9] and greater reduction in the rates of mortality and reinfarction.[10,11]

There are limited data on the efficacy and safety of primary angioplasty in octogenarians. This study analyzed the short-term and long-term outcomes, including disease severity, complications, inhospital and follow-up mortality rates, in 54 octogenarian patients with STEMI who received primary PCI at National Taiwan University Hospital (NTUH) between May 1997 and August 2004.

Methods

Patients

All octogenarian patients identified from the NTUH catheterization laboratory database who met the eligibility criteria were included. Patients had acute STEMI, defined as at least 30 minutes but < 12 hours of symptoms, and the presence of ST-segment elevation ≥ 1 mm in at least two contiguous leads or presumed new bundle-branch block on the presenting 12-lead electrocardiogram. Right ventricular infarction was diagnosed based on the finding of ST-elevation in lead V4R. Patients who had suspected STEMI but couldn't be referred for urgent coronary angiography due to prolonged resuscitation or any other causes were excluded.

Coronary angiography and primary angioplasty

After obtaining informed consent, coronary angiography was performed initially via the femoral artery according to standard clinical practice. Diseased coronary artery was defined as ≥ 50% diameter stenosis, and the left main coronary artery was classified as having two-vessel disease if the left coronary artery was non-dominant, and as having three-vessel disease if it was dominant. Multivessel disease was defined as ≥ 50% diameter stenosis in two or more major epicardial coronary arteries. The flow of the infarct-related artery (IRA) was categorized from grade 0 to grade 3 according to the Thrombolysis In Myocardial Infarction (TIMI) grading system. After diagnostic coronary angiography, the revascularization procedure was tailored to the individual patient and selected solely by the physicians. However, the family could choose conservative treatment if emergency coronary artery bypass graft (CABG) was suggested. Procedural success was defined as a reduction to residual stenosis of < 40% by balloon angioplasty or successful stent deployment at the desired position with a residual stenosis < 20% followed by TIMI grade 2 or 3 flow in the IRA.

Concomitant medical therapy

All patients were treated with aspirin 300 mg orally as the loading dosage and then 100 mg daily. Unfractionated heparin 5000 IU was given intravenously before the procedure, and then infused continuously for 48 hours. Ticlopidine 250 mg twice a day or clopidogrel 300 mg loading dose, followed by 75 mg per day was administered after stent placement for at least 1 month.

Data collection, follow-up and study endpoint

Detailed inhospital and follow-up data were collected, including serum creatine level, white blood cell (WBC) count, Killip score on hospital admission, reperfusion time, peak cardiac enzyme level and its timing, and inhospital adverse events such as sepsis, atrial or ventricular arrhythmia, and MI-related cardiac rupture or acute mitral regurgitation documented by echocardiography. Cardiogenic shock was defined as sustained hypotension with systolic blood pressure < 80 mmHg unresponsive to intravenous fluids, requiring vasopressors or intra-aortic balloon pump. Major bleeding was defined as significant blood loss from any site not caused by trauma and requiring transfusion. Left ventricular ejection fraction (LVEF) was measured after primary PCI or before discharge by the area–length method using a Sonos 4500 or 5500

(Hewlett-Packard, Palo Alto, CA, USA) with a 2–4 MHz transducer. The duration of hospital stay and causes of inhospital death were recorded. Clinical features such as baseline serum creatine, WBC count, Killip class, peak cardiac enzyme level and its timing, LVEF, and free wall rupture were analyzed for their association with mortality. Other data analyzed included congestive heart failure, defined based on the New York Heart Association classification, target lesion or target vessel revascularization (TLR/TVR), and post-hospital mortality at follow-up.

Statistical analysis

All values were expressed as mean ± standard deviation. Comparisons between parametric variables were performed using unpaired Student's *t* test, while comparisons between categorical variables were performed using the chi-square test with Yates' correction if needed. The survival rate after the episode of STEMI was plotted using the Kaplan-Meier method. All analyses were performed with SPSS version 10.0 (SPSS Inc, Chicago, IL, USA) and the Statistical Analysis System (SAS Institute Inc, Cary, NC, USA).

Table 1. Baseline characteristics of the 54 octogenarian patients with ST-elevation myocardial infarction

	n (%)
Sex (Male/Female)	35/19
Mean age ± SD (yr)	82.8 ± 2.5
Hypertension	42 (78)
Diabetes mellitus	20 (37)
Smoking	14 (26)
Hyperlipidemia	13 (24)
Prior MI	5 (9)
Prior CHF	10 (19)
Prior CVA	4 (7)
Prior PCI	4 (7)
Prior CABG	1 (2)
Aspirin	12 (22)
β-blocker	7 (13)
ACEI/ARB	8 (15)
Antiarrhythmic drugs	7 (13)
Digitalis	3 (6)
Diuretics	7 (13)
Calcium channel blockers	7 (13)
Nitrates	6 (11)
Lipid-lowering agents	1 (2)

ACEI/ARB = angiotensin converting enzyme inhibitor/angiotensin II receptor blocker; CABG = coronary artery bypass graft; CHF = congestive heart failure; CVA = cerebrovascular accident; MI = myocardial infarction; PCI = percutaneous coronary intervention; SD = standard deviation.

Results

A total of 54 octogenarian patients who met the eligibility criteria were identified from the NTUH catheterization laboratory database. The baseline characteristics of the patients are summarized in Table 1. There were 35 males and 19 females with a mean age of 82.8 ± 2.5 years (range, 80–89 years). About 80% of patients had hypertension, but less than half had a history of diabetes mellitus (37%), hyperlipidemia (24%), smoking (26%), or stroke (7%). Among the 54 patients, 9% had prior myocardial infarction (MI), 7% had previously received PCI, and only 2% had received CABG. Before the AMI episode, less than one fourth of patients used cardiovascular medications such as aspirin, β-blockers, angiotensin converting enzyme inhibitors/angiotensin II receptor blockers, antiarrhythmic drugs, digitalis, diuretics, calcium channel blockers, nitrates, or lipid-lowering agents.

Clinical and procedural features

Among the 54 patients, 30 (56%) experienced preinfarction angina, and the others presented with other symptoms such as shortness of breath or syncope. The clinical features and procedural data of the patients are summarized in Table 2. The delay from onset of symptoms to examination in the emergency room was 220 ± 167 minutes. The infarct site was in the anterior wall in 27 (50%) patients, anterolateral wall in six (11%), and inferior wall in 21 (39%). Of the 21 patients with inferior MI, three (14%) had right ventricular infarction. Initial presentation was Killip class I (free of rales and a third heart sound) in 20 (37%) patients, Killip class II (rales < 50% of lung fields

Table 2. Clinical features and procedural data of the 54 octogenarian patients with ST-elevation myocardial infarction*

Preinfarction angina	30 (56)
Arrival time (min)	220 ± 167
Reperfusion time (min)	407 ± 226
Initial WBC (1/μL)	10,630 ± 4618
Creatinine (mg/dL)	1.5 ± 1.1
Killip class	
I	20 (37)
II	9 (17)
III	2 (4)
IV	23 (43)
IRA	
LM	1 (2)
LAD	26 (48)
LCX	6 (11)
RCA	21 (39)
RV infarction	3 (14)
Pre-PCI TIMI flow	
Grade 0	28 (52)
Grade 1	11 (20)
Grade 2	12 (22)
Grade 3	3 (6)
Multivessel disease	48 (89)
Pre-PCI stenosis (%)	97 ± 7
Total PCI	43 (80)
Stenting	29 (67)
Successful PCI	41 (95)
Residual stenosis (%)	5 ± 9
Post-PCI TIMI flow	
Grade 2	3 (7)
Grade 3	38 (93)
Peak CK (U/L)	4654 ± 4336
Peaking time (hr)	14.2 ± 7.3
Failed PCI	2 (5)
CABG	6 (11)
Conservative treatment	7 (13)

**Data are presented as n (%) or mean ± standard deviation. CABG = coronary artery bypass graft; CK = creatinine kinase; IRA = infarct-related artery; LAD = left anterior descending artery; LCX = left circumflex artery; LM = left main coronary artery; PCI = percutaneous coronary intervention; RCA = right coronary artery; RV = right ventricular; TIMI = Thrombolysis In Myocardial Infarction; WBC = white blood cell.*

and with or without a third heart sound) in nine (17%), Killip class 3 (rales > 50% of each lung field) in two (4%), and Killip class IV (cardiogenic shock) in 23 (43%). One patient with sudden cardiac death had MI diagnosed by 12-lead electrocardiography after resuscitation. Multivessel disease was diagnosed by coronary angiography in 48 (89%) patients. The pre-PCI stenosis of the IRA was 97 ± 7%. TIMI flow before intervention was grade 0 in 28 (52%) patients, grade 1 in 11 (20%), grade 2 in 12 (22%), and grade 3 in three (6%). PCI was performed in 43 (80%) patients. A total of 29 stents were implanted. Successful results were achieved in 41 (95%) patients, with a reperfusion time of 407 ± 226 minutes after the onset of symptoms, and a final residual stenosis of 5 ± 9%. In the two patients with failed PCI, the guidewire could not cross the stenotic lesion in one patient who was then treated conservatively, and the no-reflow phenomenon developed in the other patient who received CABG soon thereafter. Of the 11 patients who did not receive PCI, five underwent primary CABG, and the other six were treated conservatively at their family's request due to refractory ventricular tachycardia (VT)/ventricular fibrillation (VF), old age, or other comorbid conditions associated with expected poor prognosis. Creatinine kinase peaked 14.2 ± 7.3 hours after the onset of symptoms, with a mean value of 4654 ± 4336 U/L in patients with successful PCI, and at 27.0 ± 10 hours with a mean value of 6386 ± 9191 U/L in patients with failed PCI.

Inhospital course and follow-up prognosis

The inhospital course and follow-up data are summarized in Table 3. During hospitalization, intra-aortic balloon counterpulsation was used for hemodynamic stability in 22 (41%) patients with cardiogenic shock. The measured LVEF of these patients was 43.3 ± 16.5%. Paroxysmal atrial fibrillation and VT/VF occurred in six (11%) and 12 (22%) patients, respectively. Two (4%) patients developed severe bleeding complications, which presented as intracranial and subarachnoid hemorrhage in one, and as massive upper gastrointestinal bleeding with hypovolemic shock needing transarterial embolization of the left gastric artery in the other. Both patients were discharged smoothly at 37 days and 7 days, respectively, after the MI episode. Inhospital death occurred in 23 (43%) patients, including in all of those who received conservative management and in 16 of the 47 patients (34%) who underwent successful aggressive treatment. At presentation, non-survivors had significantly ($p < 0.05$) higher Killip class (3.2 ± 1.2 *vs.* 2.0 ± 1.2), creatinine (1.9 ± 1.6 *vs.* 1.1 ± 0.3 mg/dL) and peak creatinine kinase (7012 ± 7455 *vs.* 3340 ± 2909 U/L), longer time until peaking cardiac enzyme (19.6 ± 10.5 *vs.* 14.2 ± 7.3 hours), lower LVEF (36 ± 12 *vs.* 49 ± 17%), and more free wall rupture (26 *vs.* 0%) than survivors until discharge. The mean hospital stay of non-survivors was 17 ± 44 days, and most of them (17 patients, 74%) died within 7 days after MI. The leading causes of inhospital death were profound left ventricular failure with cardiogenic shock (61%), free wall rupture with cardiac tamponade (26%), refractory VT/VF (4%), pneumonia with septic shock (4%), and acute mitral regurgitation with pulmonary edema and respiratory failure (4%). The 31 (57%) patients who were discharged smoothly had a mean hospital stay of 20 ± 22 days, and suffered from symptoms of congestive heart failure with mean New York Heart Association class 2.2 ± 0.6. At a mean of 30.1 ± 22.5 months of follow-up, eight (26%) patients had received revascularization at a mean of 7.8 ± 7.2 months after the initial treatment, including one patient with recurrent symptoms after CABG, and seven patients with TLR/TVR, among whom three patients did not receive stent implantation during the primary PCI procedure. Of the five patients who died during follow-up, cardiovascular events were considered to be the cause of death in two, including acute lung edema resulting in respiratory failure at 68 days in one, and sudden cardiac death at 1 year post-discharge in the other. Another three patients died of non-cardiovascular causes, including pneumonia with septic shock at 3 months in one, ischemic bowel disease presenting as acute abdomen at 11 months in one, and gastric cancer at 1 year post-discharge in one.

Table 3. Inhospital and follow-up course in 54 octogenarian patients with ST-elevation myocardial infarction*

VT/VF	12 (22)
PAF	6 (11)
CAVB	11 (20)
IABP	22 (41)
LV ejection fraction (%)	43.3 ± 16.5
Severe bleeding	2 (4)
Major bleeding	1 (50)
Intracranial hemorrhage	1 (50)
Inhospital deaths	23 (43)
Mean hospital stay (d)	17 ± 44
Causes of death	
Profound cardiogenic shock	14 (61)
Free wall rupture	6 (26)
Refractory VT/VF	1 (4)
Septic shock	1 (4)
Acute mitral regurgitation	1 (4)
Survived to discharge	31 (57)
Mean hospital stay (d)	20 ± 22
NYHA class	2.2 ± 0.6
Revascularization	8 (26)
Mean time of revascularization (mo)	7.8 ± 7.2
Target vessel revascularization	7 (88)
Follow-up mortality	5 (16)
Causes of death	
Cardiovascular	2 (40)
Septic shock	1 (20)
Acute abdomen	1 (20)
Gastric cancer	1 (20)

**Data are presented as n (%) or mean ± standard deviation. CAVB = complete atrioventricular block; IABP = intra-aortic balloon pump; LV = left ventricular; NYHA = New York Heart Association; PAF = paroxysmal atrial fibrillation; VT/VF = ventricular tachycardia/ventricular fibrillation.*

Kaplan-Meier curve for analysis of survival rate

The Kaplan-Meier curve of the overall survival of the 54 octogenarians with STEMI eligible for primary PCI is shown in the Figure. Inhospital mortality ($n = 23$, 43%) was responsible for most of the initial decline in survival within 2 months of the AMI episode. Another five patients among the 31 survivors who were discharged died within 1 year.

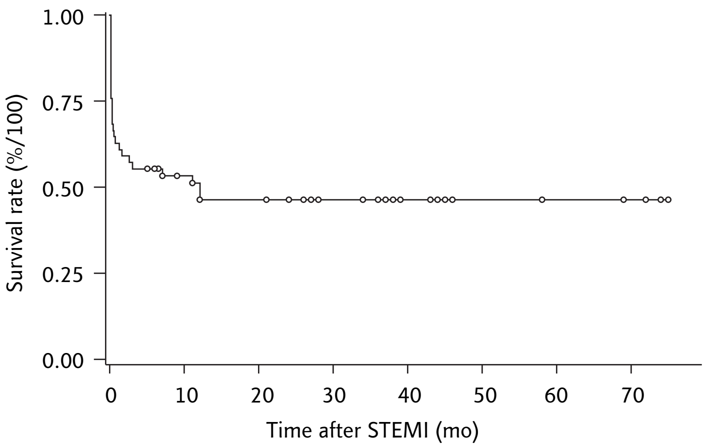

Figure. Kaplan-Meier survival estimates of 54 octogenarian patients with ST-elevation myocardial infarction (STEMI).

Discussion

Primary angioplasty is increasingly advocated as an approach that should supersede thrombolysis for the treatment of acute STEMI,[12,13] especially in the elderly.[14,15] Although risks to octogenarians undergoing PCI are two- to fourfold higher than in younger patients,[16] a randomized trial by De Boer et al also disclosed that primary angioplasty, compared with intravenous streptokinase treatment, reduced the 30-day composite incidence of death, reinfarction or stroke from 29% to 9% in patients > 75 years of age.[17]

In this study, nearly half (43%) of octogenarians with acute STEMI initially presented with cardiogenic shock, a substantially higher percentage than the average of 7–10% reported in the general population[18,19] in studies from the United States. Only eight (35%) of these patients survived to discharge, with an inhospital mortality rate of 65% even after revascularization, which is lower than the previously reported 30-day mortality rates in the United States of 44% in patients aged ≥ 75 years[20] and 70% in those aged ≥ 80 years in Italy.[15] As a part of the aging process, coronary arteries are prone to dilation, tortuosity, medial calcification and impairment of endothelial function,[21] in addition to reduced cardiac and overall physiologic reserve. All of these factors may contribute to the high incidence of multivessel (89%) or complicated coronary artery disease resulting in increased difficulty[22,23] of angioplasty in octogenarians. In this series, coronary intervention was considered inappropriate after diagnostic angiography in 20% of patients. There was also a high prevalence (43%) of cardiogenic shock in octogenarian patients with AMI.

Although the high success rate (95%) of primary coronary intervention in this study was similar to previous studies,[15] the mean hospital stay was still prolonged and the inhospital mortality rate (43%) was much higher than previously reported. The main causes of inhospital death were profound left ventricular failure with cardiogenic shock (61%) and free wall rupture (26%). Aged hearts are more prone to ischemic injury because of impaired ischemic preconditioning[24] and decreased angiographic presence of collaterals to the IRA.[25] Delay in time to reperfusion may result in impaired myocardial perfusion and greater injury,[25] which contribute to poor inhospital prognosis in this population. Therefore, cardiogenic shock, free wall rupture, and life-threatening arrhythmias are more likely to occur in elderly patients[26] and lead to a worse short-term prognosis.[27,28]

Among the 31 survivors who received reperfusion therapy (CABG, $n = 2$) and were discharged, five (16%) patients died within 1 year due to cardiovascular events or other non-cardiac etiology. This is consistent with the findings of Singh et al that the long-term prognosis following successful angioplasty was similar to that of the general population.[29] Revascularization was needed in eight (26%) of these patients at a mean of 7.8 ± 7.2 months. The Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial found that coronary stenting reduced the 1-year rate of ischemic target revascularization (7.0% *vs.* 17.6%; $p < 0.001$) compared with balloon angioplasty alone among elderly (≥ 65 years) patients.[30] The older population and the 67% stent implantation rate in this study might explain the higher rates of revascularization in comparison to the CADILLAC study.

Although elderly patients are at higher risk of stroke and major bleeding than younger patients, the incidence (4%) of severe bleeding was acceptable in this study of octogenarian patients who received primary angioplasty when compared to the 0–8% rate reported previously in the elderly.[31,32]

Study limitations

The major limitation of this study was the lack of a control group, which would have been difficult to form because the absolute patient number was small even when collected over a relatively long study period, and other standard aggressive treatment such as thrombolytic therapy was rarely indicated. Thus, the results and findings must be interpreted as descriptive as opposed to demonstrating effectiveness. This study supports, however, that this age group benefits from primary angioplasty for AMI. Another limitation was the inclusion only of patients in the catheterization laboratory database. The inclusion of some patients with STEMI and sudden cardiac death or death on arrival might have caused a major selection bias leading to underestimation of the frequency of adverse outcomes. Nevertheless, the patients included in this study represented a high-risk population, and the data are likely to be representative of outcomes in this high-volume catheterization laboratory with experienced operators.

Conclusion

In the era of primary angioplasty, octogenarians with acute STEMI still have a high probability of complex coronary stenoses, worse initial presentation, prolonged hospital stay, and higher overall mortality. Whether newer pharmacotherapy such as antiplatelet agents, device therapy such as embolic protecting filters or thrombectomy catheters, or drug-eluting stents can improve the prognosis of this population warrants further investigation.

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